1-2007

Update - January 2007

Loma Linda University Center for Christian Bioethics

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Update

Volume 21, Number 3 (January 2007)

Stem Cells, Embryos, and Ethics: Is There a Way Forward?

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Adapted from the Health and Faith Forum: Bioethics and Wholeness Grand Rounds presentation January 10, 2007

We are at a crucial moment in the process of scientific discovery. The dramatic advances in molecular biology throughout the 20th century have culminated in the sequencing of the human genome and increasing knowledge of cell physiology and cytology. These studies were accomplished by breaking down organic systems into their component parts. Now, however, as we move on from genomics and proteomics to discoveries in developmental biology, we have returned to the study of living beings. When applied to human biology, this inquiry reopens the most fundamental questions concerning the relationship between the material form and the moral meaning of developing life.

The current conflict over embryonic stem (ES) cell research is just the first in a series of difficult controversies that will require us to define with clarity and precision the moral boundaries we seek to defend. Human-animal chimeras, parthenogenesis, projects involving the laboratory production of organs—and a wide range of other emerging technologies will continue to challenge our definitions of human life. These are not questions for science alone, but for the full breadth of human wisdom and experience.

The scientific arguments for going forward with this research are strong. The convergence of these advancing technologies is delivering unprecedented powers for research into the most basic questions in early human development. Beyond the obvious benefit of understanding the biological factors behind the estimated 150,000 births with serious congenital defects per year, it is becoming increasingly evident that certain pathologies that are only manifest later in life are influenced or have their origins in early development. Furthermore, fundamental developmental processes (including the formation and functioning of stem cells), and their disordered dynamics, seem to be at work in a range of adult pathologies including some forms of cancer.

Yet, from the moral and social perspective there are serious concerns.

It is important to acknowledge the many scientific projects for which human embryos could be used. Beyond their destruction for the procurement of embryonic cells, some individuals fear the industrial scale production of living human embryos for a wide range of research in natural development, toxicology, and drug testing.

Lord Alton, a member of the House of Lords in the United Kingdom, told me that they estimate more than 100,000 human embryos have already been used in scientific experimentation in Britain.

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Beyond that, there is concern about the commodification and commercialization of eggs and embryos, and worry about the implications of ongoing research to create an artificial endometrium (a kind of artificial womb) that would allow the extracorporeal gestation of cloned embryos to later stages for the production of more advanced cells, tissues, and organs.

Furthermore, from a social perspective, do we really want to have red state medicine/blue state medicine? The emerging patchwork of policies on the state level threatens to create a situation in which a large percentage of patients will enter the hospital with moral qualms about the foundations on which their treatments have been developed. What was traditionally the sanctuary of compassionate care at the most vulnerable and sensitive moments of human life is becoming an arena of controversy and conflict.

Clearly, both sides of this difficult debate are defending important human goods—and both of these goods are important for all of us. A purely political solution will leave our country bitterly divided, eroding the social support and sense of noble purpose that is essential for the public funding of biomedical science. While there are currently no federally legislated constraints on the use of private funds for this research, there is a consensus opinion in the scientific community that without NIH support for newly created embryonic stem cell lines, progress in this important realm of research will be severely constrained. The current conflict in the political arena is damaging to science, to religion, and to our larger sense of national unity. The way this debate is proceeding is, in my opinion, completely contrary to the positive pluralism that is the strength of our democracy.

"Clearly, both sides of this difficult debate are defending important human goods—and both of these goods are important for all of us."

What is needed is to draw back from the polarized positions of political rhetoric and to respectfully reflect on the meaning of the moment we are in.

In the spirit of such a dialogue, and in the hope that it might lead us toward a resolution of our difficult national impasse over embryonic stem cell research, I offer the perspective that follows.

Moral meaning of emerging life

Any evaluation of the moral significance of human life must take into account the full procession of continuity and change that is essential for its development. With the act of conception, a new life is initiated with a distinct genetic endowment that organizes and guides the growth of a unique and unrepeatable human being.

The gametes (the sperm and egg), although alive as cells, are not living beings: they are instrumental organic agents of the parents. The joining of the gametes brings into existence an entirely different kind of entity, a living human organism. With regard to fundamental biological meaning (and moral significance), the act of fertilization is a leap from zero to everything.

In both structure and function, the zygote (the one-cell embryo) and subsequent embryonic stages differ from all other cells or tissues of the body; they contain within themselves the organizing principle for the full development of a human being. The very word organism implies organization—an overarching principle that binds the parts and processes of life into a harmonious whole. As a living being, an organism is an integrated, self-developing, and self-maintaining unity under the governance of an immanent plan.

For an embryonic organism, this implies an inherent potency, an engaged and effective potential with a drive in the direction of the mature form. By its very nature, an embryo is a developing being. Its wholeness is defined by both its manifest expression and its latent potential; it is the phase of human life in which the "whole" (as the unified organismal principle of growth) precedes and produces its organic parts. The philosopher Robert Joyce explains: "Living beings come into existence all at once and then gradually unfold to themselves and to the world what they already, but only incipiently, are."[1] To be a human organism is to be a whole living member of the species *Homo sapiens*, with a human present and a human future evident in the intrinsic potential for the manifestation of the species' typical form. Joyce continues: "No living being can become anything other than what it already essentially is."

It is this implicit whole, with its inherent potency, that endows the embryo with continuity of human identity from the moment of conception and therefore, from this perspective, inviolable moral status. To interfere in its development is to transgress upon a life in process. The principle of this analysis applies to any entity that has the same potency as a human embryo produced by natural fertilization, regardless of whether it is the product of *in vitro* fertilization (IVF), cloning, or other processes.

Accrued moral status

The major alternative to the view that an embryo has an inherent moral status is the assertion that moral status is an accrued or accumulated quality related to some dimension of morphology or function.

The three arguments currently given in support of a 14 day limit on embryo research—lack of differentiation, lack of individuation, and pre-implantation status—are based on a kind of "received tradition" that dates back to the 1986 Warnock Commission in the United Kingdom. But this commission explicitly acknowledged the continuous nature of embryonic development, stating: "There is no particular part of the developmental process that is more important than any other." In a recent memoir, Mary Warnock discussed the utilitarian grounding of her commission's analysis, acknowledging that her committee's task was "to recommend a policy which might allow the sort of medical and scientific progress which was in the public interest."[2] Indeed, recent advances in embryology do not support this commission's conclusions.

Differentiation

The argument on differentiation is based on the idea that before gastrulation (which begins around the 12th to 14th day with the formation of the primitive streak (Fig. 1), the embryo is an inchoate clump of cells with no actuated drive in the direction of distinct development.

It is argued that the undifferentiated quality of the blastocyst (the four-five day embryo) justifies its disaggregation for the procurement of stem cells, while the evident organization at gastrulation reveals an organismal integrity that endows inviolable moral status to all subsequent stages of

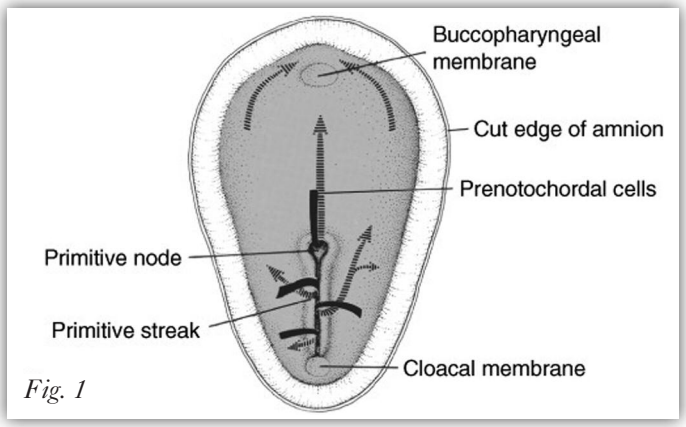

Fig. 1

embryological development.

Scientific evidence, however, supports the opposing argument—that from conception there is an unbroken continuity in the differentiation and organization of the emerging individual life.

- The anterior-posterior axis appears to be already established within the zygote (the one-cell stage).
- The earliest embryonic cell divisions (at least at by the four-cell stage) exhibit differential gene expression.
- The unequal cytoplasmic concentrations of cell constituents in the early embryo suggest distinct cellular fates.

All this implies that the changes at gastrulation do not represent a discontinuity of ontological significance (a change in the nature of being), but merely the visibly evident culmination of more subtle developmental processes at the cellular level that are driving in the direction of organismal maturity.[3] These new scientific perspectives were documented in a July 2002 article in *Nature*: "The mammalian body plan starts being laid down from the moment of conception…a surprising shift in embryological thinking."

Twinning

Another argument for accrued moral status is that, as long as an embryo is capable of giving rise to a twin, it cannot be considered to have the moral standing of an individual.

Yet monozygotic twinning, which occurs in just one in 240 births, does not appear to be either an intrinsic drive or a random process within embryogenesis. Rather, it results from a disruption of normal development by a mechanical or biochemical disturbance of fragile cell relationships. This provokes a compensatory repair, but with the restitution of integrity within two distinct trajectories of embryological development.

In considering the implications of twinning for individuation, one might better ask the question from the opposite perspective. What keeps each of the cells of the early embryo from becoming a full embryo? Clearly, crucial relational dynamics of position and intercellular communication are already at work, establishing the unified pattern of the emerging individual.

From this perspective, twinning is not evidence of the absence of an individual, but of an extraordinary power of compensatory repair that reflects more fully the potency of the individual drive to fullness of form even in the earliest stages of embryonic human life.

Implantation

Some have argued that the implantation of the embryo within the uterine lining of the mother constitutes a moment of altered moral status.

Fertilization occurs in the fallopian tubes. The embryo floats down into the uterus and begins to implant in the uterine wall around the sixth–seventh day. All along this journey,

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the diffusion of essential nutrients and growth factors sustains the life and nourishes the growth of the developing embryo. Implantation and the development of the placenta simply extend this relationship between mother and embryo, with an internal circulation as the embryo gets too large to be nourished by direct diffusion.

Implantation, then, must be viewed as just another step in a continuum of ongoing intimate dependence, all occurring along the trajectory of natural development that begins with conception and continues into infancy. This continuity implies no meaningful moral marker at implantation.

Function

Most other arguments relate in some way to the onset of a specific function or capacity. Arguments for a change in moral status based on function are at once the most difficult to refute and to defend.

The first and most obvious problem is that the essential functions (and even their minimal criteria and age of onset) are diverse and arbitrarily assigned. Generally they relate to the onset of sentience—awareness of pain, or some apparently unique human cognitive capability such as consciousness.

This approach raises a number of disturbing ethical questions.

- If human moral worth is based on actual manifest functions, then does more of that function give an individual life a higher moral value?
- And what are we to make of the parallel functional capacities in animals that we routinely sacrifice for food and medical research?
- Furthermore, what becomes of human moral status with the degeneration or disappearance of such functions? While we might argue that our relational obligations change along with changes in function, such as occur with senile dementia, we would not sanction a utilitarian calculus and the purely instrumental use of such persons no matter how promising the medical benefits might be.

More fundamentally, from a scientific perspective, there is no meaningful moment when one can definitively designate the biological origins of a human characteristic such as consciousness. The human being is an inseparable psychophysical unity. Our thinking is in and through our bodily being, and thus the roots of our consciousness reach deep into our development. The earliest stages of human development serve as the indispensable and enduring foundations for the powers of freedom and self-awareness that reach their fullest expression in the adult form.

With respect to fundamental moral status therefore, the human being is an embodied being whose intrinsic dignity is inseparable from its full procession of life and always present in its varied stages of emergence.

This conclusion is consistent with 2,500 years of medical science—as recently as 1948, the Physician's Oath in the Declaration of Geneva, echoing the enduring traditions of Hippocratic medicine, proclaimed: "I will maintain the utmost respect for human life from the time of conception. …"

As we descend into an instrumental use of human life, we destroy the very reason for which we were undertaking our new therapies; we degrade the humanity we were trying to heal.

In vitro fertilization embryos

This brings us to the dilemma of the moral status of an estimated one million embryos left over from *in vitro* fertilization (IVF). Created to give life, they are now suspended in time and space and the uncertainty of a conflicted fate.

In this canister (Figure 2) in the Assisted Reproduction Technologies clinic at Stanford are 300 embryos. The water in their cells has been replaced with glycerol, and they are immersed in liquid nitrogen at a temperature of minus 200 degrees Celsius. (I joke with my friend, the director of the lab, that this must be the densest population in human history.)

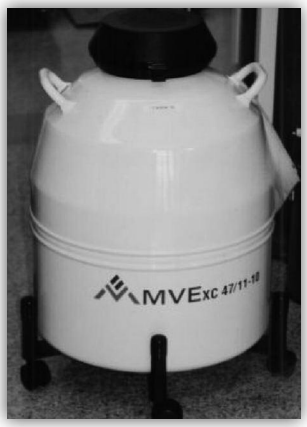

Fig. 2

But the future of these embryos is a poignant problem. In some cases, such embryos have been implanted as long as 12 and a half years after freezing, including one born seven and a half years after its twin. In other cases, there have been custody battles over the frozen embryos after divorce, and even a dispute over inheritance when a wealthy couple died in an airplane crash and left several embryonic hiers with numerous couples stepping forward and offering to adopt them. But most of these one million frozen embryos do not have such privileged prospects. They are castoffs, destined to be discarded or disaggregated in the service of medical science.

And this is a warning to us of how even the best intentions of our science, unconstrained by the forethought of moral consideration, slip slowly along the gradient of utility. Each of these embryos, once the precious promise of a happy baby, is now relegated to the category of mere matter, raw material in a larger program of scientific progress.

However much we may agree or disagree with the process that put them there, we should acknowledge that this is a difficult dilemma. Produced with a healing purpose, the good intentions of overcoming the sorrow of infertility, they are now abandoned to a project of a completely different character. Some say that if there is a moral problem, it is upstream in the process that put them there, and that now, since they are destined to die, what further harm can be done? As a pragmatic people, many Americans feel the weight of this argument. And, if we fail to develop a morally acceptable alternative source of embryonic stem cells, I suspect that is where our national policy may settle.

Yet, even if use of these embryos becomes accepted policy and practice, we should be aware of something more complicated that is below the surface: There has been a slow but steady shift in our underlying attitude toward human life. As we gain the powers of comprehension and control over our most basic biology, there is a transformation—not just in our physical being, but in our whole sense of who we are, and of our place and purpose within the natural order.

"As we descend into an instrumental use of human life we destroy the very reason for which we were undertaking our therapies…"

As we take increasing instrumental control over natural life processes, our attitude changes and we lose the sense of cautionary reverence and respect. With each step, however benevolent the initial intention, there is a moral danger, a fracturing of matter and meaning that breaks the coherence and natural connections of life. With each step, the original radiance and vitality of the cosmos, its order, beauty, and coherent moral meaning are obscured by the conviction that all of living nature is mere matter and information to be reshuffled and reassigned for the projects of the human will.

This instrumental use of life reaches its most ominous extension as we relegate the human embryo to the status of a resource, as raw material in the service of our project in the mastery over nature. Such an instrumental use of early human life opens a doorway down a long corridor indeed.

For one thing, many of these embryos are not at the developmental state for harvesting embryonic stem cells and would have to undergo further laboratory culture to the blastocyst stage. Will we not want to use some for experiments to perfect the culture medium? And while we are at it, there are many other studies that could be done on early embryos to help perfect IVF.

Thirty years ago, when IVF first came on the scene, there was a difficult debate in Congress over support of research that involves the destruction of human life. This debate culminated in 1996 with the passage of the Dickey Amendment, which forbids federal funding for projects that endanger or destroy human embryos. As with abortion, IVF, involving the creation and implantation or disposal of embryos, would be a matter of personal choice done with private funds.

Will we now retreat and override this decision—or is only embryonic stem cell research urgent enough to justify an exception to this long-standing federal policy? Furthermore, even if we endorse this course of action, the 14-day limit on the use of human embryos will not hold since it does not stand up to logical argument. As discussed above, the designation of 14 days as the moral boundary for embryo experimentation is in the category of a "received tradition," almost a superstition in the sense that it is a belief in a change of state without a discernible cause. As a moral marker, 14 days makes no sense; it is arbitrarily set and therefore vulnerable to transgression through the persuasive promise of further scientific benefit.

Beyond cells

And it is becoming increasingly apparent that the promise of stem cells lies beyond simple cell cultures and cell replacement. The technological goal is to produce more advanced cell types and even tissues, organs, and possibly limb primordia. Producing such complex tissues and organs may require the intricate cell interactions and microenvironments now available only through natural gestation.

During embryogenesis, differentiation and organ formation unfold within the fragile spatio-temporal induction of a highly specific sequence of cell signaling—different signals coming from different sides and in a perfect synchrony of process.

Consider the formation of the human hand. It begins as a small bud induced off the trunk of the embryo; then through an extraordinary orchestration of cell interactions, it progressively unfolds toward its functional form. But once initiated (after about the fifth or sixth week of embryogenesis, Figure 3), the limb bud can actually be severed from the embryo and, given the right environment, will continue its momentum of development as an independent unit.

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I have seen just such a hand in the bottom of a test tube. The tiny limb bud, snipped from the fetal remains of a five week old aborted fetus, was implanted into the abdominal cavity of an SCID mouse (a special kind of mouse that won't reject the tissue), and grown till it was about one-quarter inch wide. I looked down on that little hand and I thought to myself—this is fantastic; one day we may grow limbs for people with congenital malformations, or injuries and amputations. But at the same time I thought—this was going to be someone's little hand, that tender little newborn hand that lays across his mother's breast while nursing.

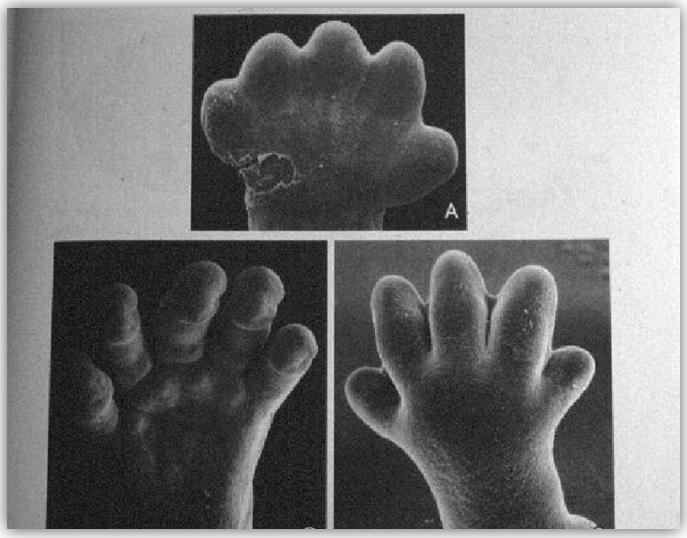

Fig. 3

But if we might one day grow human limbs, we might even more easily grow other organs—kidneys, livers, and hearts. Scientists in Israel have already established that human kidney primordia taken from seven-to-eight-week-old aborted fetuses can be successfully grown in mice—a feat proclaimed as "a breakthrough that might one day help save thousands of patients waiting for transplants." (There are 50,000 people in the United States alone on dialysis, waiting for kidney transplants—an estimated 17 deaths a day are due to the inadequate organ supply.) Furthermore, several years ago, it was announced that a scientist in China successfully sustained *in vitro* a human heart severed from its source in a seven-week-old aborted fetus.

The benefits of implanting embryos in order to employ the developmental dynamics of natural embryogenesis for the production of limb and organ primordia seem self-evident.

The implantation of cloned embryos (either into the natural womb or possibly an artificial endometrium) for the production of patient-specific tissue types to bypass problems of immune rejection would further extend the logic of the instrumental use of developing life.

The public pressure that has already been brought to bear on the politics of stem cells and cloning by patient advocacy groups has provoked such a sense of promise that it may propel the argument for allowing such gestation of cloned human embryos.

Over the past four years, I have talked with hundreds of people, including many scientists, who say that they would find such a practice (that is, the implantation of a cloned embryo) acceptable to save the life of a dying child.

Different people have different limits to the duration of gestation they find morally acceptable, but in light of the current sanction of abortion up to and beyond the end of the second trimester, it is difficult to argue that the creation, gestation, and sacrifice of a clone to save an existing life is a large leap in the logic of justification. The argument is made that if abortion is legal—that is, if a developing life can be terminated with no reason given—then why not for a good reason? One must admit there is a certain perverse logic to this argument.

White paper

In light of the arguments given above that human moral worth is based on a continuity of embodied form from fertilization to natural death, it would seem that we are at an irresolvable impasse. If embryonic stem cells can be obtained only by the destruction of human embryos, this may, in fact, be the case. But last May, a white paper by the President's Council on Bioethics suggested otherwise. This report describes four proposals put forward as possible means of obtaining embryonic stem cells without the creation and destruction of human embryos.

As the author of one of the proposals, altered nuclear transfer, I would like to draw on this to discuss the scientific advances and moral reasoning that may lead us to a technological solution to our national conflict.

Altered nuclear transfer

As described above, natural conception signals the activation of the organizing principle for the self-development and self-maintenance of the full human organism. In the language of stem-cell biology, this capability is termed "totipotency," the capacity to form the complete organism. A naturally fertilized egg, the one cell embryo, is totipotent.

In contrast, the term "pluripotency" designates the capacity to produce all the cell types of the human body, but not the coherent and integrated unity of a living being. Embryonic stem cells are merely pluripotent. This is a difference between the material parts and the living whole.

Altered nuclear transfer (ANT) would draw on the basic technique of SCNT (popularly known as "therapeutic cloning") but with an alteration such that pluripotent stem

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cells are produced without the creation and destruction of totipotent human embryos.

In standard nuclear transfer, the cell nucleus is removed from an adult body cell and transferred into an egg cell that

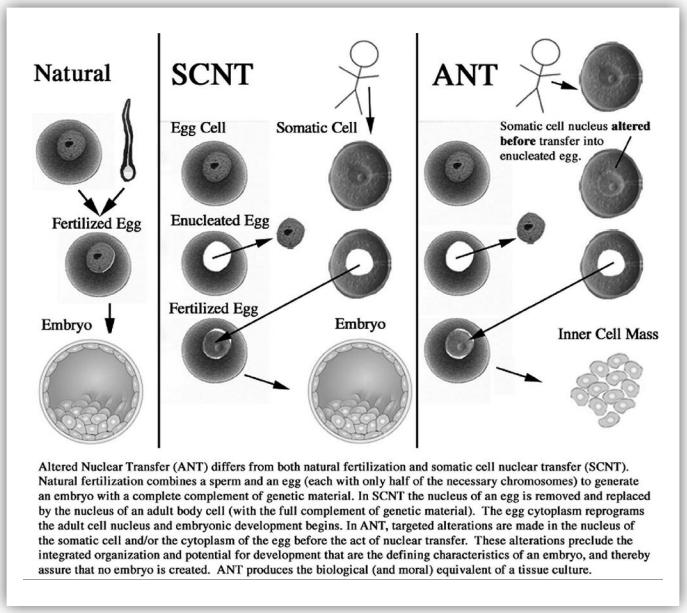

Fig. 4

first has its own nucleus removed. The egg then has a full set of DNA and, after it is electrically stimulated, starts to divide like a naturally fertilized egg. This is how Dolly, the sheep, was produced.

Altered nuclear transfer uses the technology of nuclear transfer but with a preemptive alteration that assures that no embryo is created. The adult body cell nucleus or the enucleated egg's contents (or both) are first altered before the adult body cell nucleus is transferred into the egg. The alterations cause the adult body cell DNA to function in such a way that no embryo is generated, but pluripotent stem cells are produced.

There is natural precedent for such a project. In normal conception, fertilization signals the activation of the organizing principle for the self-development of the full human organism.

But without all of the essential elements—the necessary complement of chromosomes, proper epigenetic configuration, and the cytoplasmic factors for gene expression—there can be no living whole, no organism, and no human embryo. Recent scientific evidence suggests incomplete combinations of the necessary elements—"failures of fertilization"—are the fate of many, perhaps most, of early natural initiations in reproduction.

Failures of fertilization

It is important to realize that many of these naturally occurring failures of fertilization may still proceed along partial trajectories of organic growth without being actual organisms. For example, certain grossly abnormal karyotypes (including haploid genomes, with only half the natural number of chromosomes) will form blastocyst-like structures but will not implant.

Even an egg without a nucleus, when artificially activated, has the developmental power to divide to the eight-cell stage, yet clearly is not an embryo—or an organism at all. The mRNA for the protein synthesis that drives these early cell divisions is generated during the maturation of the egg and then activated after fertilization. Like a spinning top, the cells contain a certain biological momentum that propels a partial trajectory of development; but unlike a normal embryo, they are unable to bootstrap themselves into becoming an integrated and self-regulating organism.

Some of these aberrant products of fertilization that lack the qualities and characteristics of an organism appear to be capable of generating ES cells or their functional equivalent. Mature teratomas are benign tumors that generate all three primary embryonic cell types, as well as more advanced cells and tissues, including partial limb and organ primordia—and sometimes hair, fingernails, and even fully formed teeth. (The white opacities in this x-ray are adult-size molars, Figure 5.) Yet these chaotic, disorganized, and nonfunctional masses are like a bag of jumbled puzzle parts, lacking entirely the structural and dynamic character of organisms. Neither medical science nor the major religious traditions have ever considered these growths to be "moral beings" worthy of protection; yet they produce embryonic stem cells.

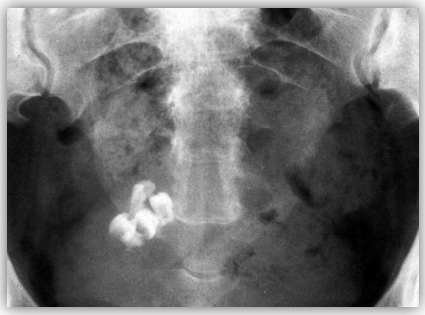

Fig. 5

These benign ovarian tumors appear to be derived by spontaneous development of activated eggs. The disorganized character of teratomas appears to arise, not from changes in the DNA sequence, but from genetic imprinting—an epigenetic modification that affects the pattern of gene expression (keeping some genes turned off and others on). In natural reproduction, the sperm and egg have different but complementary patterns of imprinting, allowing a coordinated control of embryological development. When an egg is activated without a sperm, the trophectoderm (the outer layer in a natural embryo—sometimes called the trophoblast) and its lineages fail to develop properly. In the absence of the complementary genetic contribution of

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the male, the activated egg is simply inadequately constituted to direct the integrated development characteristic of human embryogenesis.

Systems biology

This example points to another new dimension of our advancing knowledge. Through systems biology, we are beginning to recognize how even a small change of one gene can affect the entire balance of an enormous network of biochemical processes necessary to initiate and sustain the existence of a living being.

Systems biology offers us the view of an organism as a dynamic whole, an interactive web of interdependent processes that express emergent properties not apparent in the biochemical parts. Within this dynamic self-sustaining system is the very principle of life, the organizing information and coordinated coherence of a living being. With the full complement of coordinated parts, an organismal system subsumes and sustains the parts; it exerts a downward causation that binds and balances the parts into a patterned program of integrated growth and development. Partial organic subsystems (cells, tissues, and organs) that are components of this larger whole, if separated or separately produced, may temporarily proceed forward in development. But without the coherent coordination and robust self-regulation of the full organism, they will ultimately become merely disorganized cellular growth.

ANT proposes that small, but precisely selected alterations will allow the harnessing of partial developmental trajectories apart from their full natural context in order to produce ES cells.

Cdx2

Altered nuclear transfer is a broad concept with a range of possible approaches; there may be many ways this technique can be used to accomplish the same end.

One variation involves the deletion or silencing of a gene essential at the most primary level of coordinated organization. As described in a January 2006 paper in the journal *Nature*, stem-cell biologist Rudolf Jaenisch has established the scientific feasibility of this approach in a series of dramatic mouse model experiments in which he procured fully functional embryonic stem cells from a laboratory construct that is radically different in developmental potential than a normal embryo.[4]

Using the technique of RNA interference, he was able to reversibly silence the gene Cdx2 in the donor nucleus before nuclear transfer to the enucleated egg. And a study just two months ago in the journal *Science* suggests that it

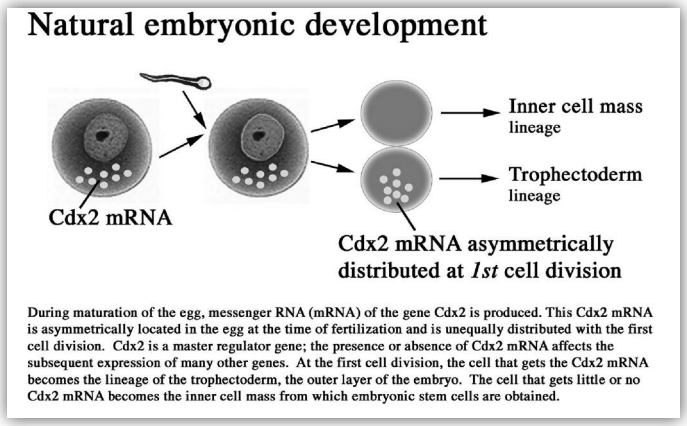


Fig. 6

may be possible to achieve the goals of ANT through the preemptive silencing of Cdx2 in the egg even before the act of nuclear transfer, thereby producing the biological (and moral) equivalent of an inner cell mass tissue culture. This article showed that in mice, mRNA for Cdx2 is present in the egg and asymmetrically distributed in the first cell division after fertilization. This asymmetric distribution of Cdx2 directs the cells at the two-cell stage to form two distinct cell lineages. One of the cells at the two-cell stage goes on to become the trophectoderm and forms the outer layer of the embryo (and later the extra-embryonic membranes, including the placenta). The other cell forms the "inner cell mass," which is the source of embryonic stem cells. By selective silencing of Cdx2, the authors were able to produce an unorganized mass composed exclusively of cells with the character of inner cell mass.

This is the organic equivalent of a model airplane kit without the glue; you have parts but no capacity to form a coherent whole. The gene Cdx2 has been shown in mouse models to be essential for the early integration of organismal function. In the absence of expression of this gene, as with a teratoma, the trophectoderm fails to grow and there is only partial and unorganized cellular process. Lacking one of the two essential cell types, it is the equivalent of trying to sing a duet with only one voice. The coordinated interactions that are essential for embryonic development are simply not possible. Nonetheless, an inner cell mass is produced from which functional embryonic stem cells can be extracted.

It is important to recognize that the improper development of the trophectoderm is not reasonably considered a defect within a part, but rather a failure in the formation of the whole. An early embryo does not have parts in quite the same sense as an adult organism, or even as a later-stage embryo just a few days or weeks later. Natural embryogenesis is, by definition, the period during which the whole, as the unified principle of growth, produces the parts. The differentiation of parts during early embryogenesis lays down the fundamental axes, body plan, and pattern of inte-

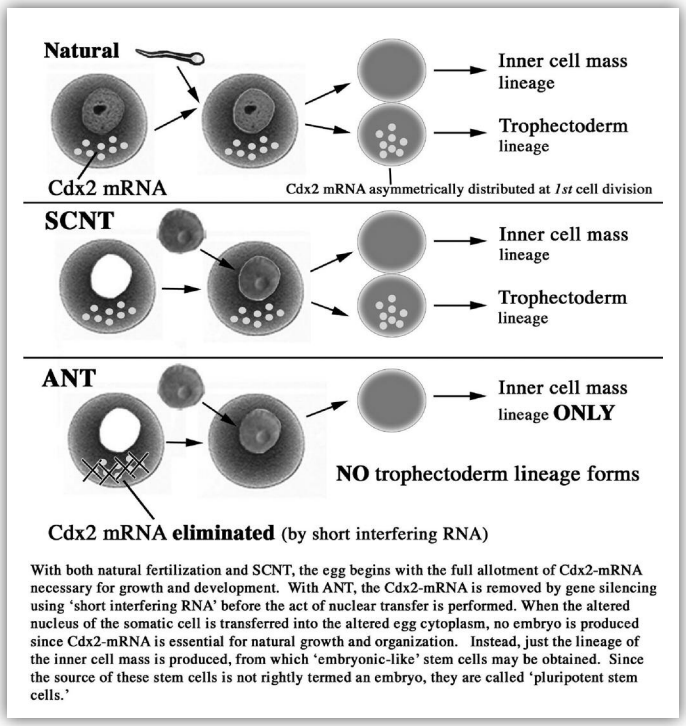
grated organogenesis. An embryo does not have a central integrating part like the brain; rather, the essential being is the whole being. At this stage, a critical "deficiency" is more rightly considered an "insufficiency"—not a defect in a being, but an inadequacy at such a fundamental level that it precludes the coordinated coherence and developmental potential that are the defining characteristics of an embryonic organism. In testimony to a U.S. Senate subcommittee on stem-cell research, Dr. Jaenisch stated: "Because the ANT product lacks essential properties of the fertilized embryo, it is not justified to call it an 'embryo.'"[5]

Many scientists, moral philosophers, and religious authorities (including some of the most conservative evangelical and Catholic leaders) have expressed strong encouragement for further exploration of this project. Of course, additional animal studies including some with non-human primates, must precede any translation of these findings into practice with human cells.

Advantages of ANT

ANT, in its many variations, could provide a uniquely flexible tool and has many positive advantages that would help advance stem cell research.

- Unlike the use of embryos from IVF clinics, ANT would produce an unlimited range of genetic types for the study of disease, drug testing, and possibly generation of therapeutically useful cells.
- By allowing controlled and reproducible experiments, ANT would provide a valuable research tool for a wide range of studies of gene expression, imprinting, and intercellular communication. Furthermore, the basic research essential to establishing the ANT technique would advance our understanding of developmental biology and might serve as a bridge to transcendent technologies, such as direct reprogramming of adult cells.
- Moreover, as a direct laboratory technique, ANT would unburden embryonic stem-cell research from the additional ethical concerns of the "leftover" IVF embryos, including the attendant clinical and legal complexities in this realm of great personal and social sensitivity.



With both natural fertilization and SCNT, the egg begins with the full allotment of Cdx2-mRNA necessary for growth and development. With ANT, the Cdx2-mRNA is removed by gene silencing using 'short interfering RNA' before the act of nuclear transfer is performed. When the altered nucleus of the somatic cell is transferred into the altered egg cytoplasm, no embryo is produced since Cdx2-mRNA is essential for natural growth and organization. Instead, just the lineage of the inner cell mass is produced, from which 'embryonic-like' stem cells may be obtained. Since the source of these stem cells is not rightly termed an embryo, they are called 'pluripotent stem cells.'

Fig. 7

The one remaining link with IV—the procurement of oocytes—is a subject of intense scientific research, and there appear to be several prospects for obtaining eggs without the morally dubious and expensive hormonally induced superovulation of female patients. These include the use of eggs left over from IVF, the laboratory maturation of eggs cultured from ovaries obtained after surgical removal or from cadavers, and possibly the direct production of eggs from embryonic stem cells (a feat already accomplished with mouse cells).

Conclusion

We are at a crucial moment in the progress of science and civilization. Advances in biology have delivered new powers with extraordinary potential for positive application in both basic research and clinical medicine. Yet, at the same time, these new possibilities challenge the most fundamental moral principles on which our society is based. Clearly, both sides of this difficult debate over embryonic stem cell research are defending something important to all of us. Without a resolution that sustains social consensus, there will be a series of continuing conflicts as our science challenges us with further dilemmas at the boundaries of human life.

English author G.K. Chesterton had a metaphor that may inform our current situation. Little boys are playing soccer on an island, but at the very edges of the field, cliffs go down hundreds of feet to the waves crashing against the rocky shore. The boys are playing, but only in the middle 20 yards—no one wants to do a corner kick. Then someone comes and builds a sturdy fence right at the edges of the field: now they can play within the full field without fear of falling off the cliff.

Our current conflict is like this: Science is stalled across a broad front. If we can define with clarity and precision the moral boundaries we are trying to defend, we might open a wider arena of legitimate study without fear of the grave dangers posed by breach of the basic moral principles that sustain

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"Stem Cells, Embryos, and Ethics" continued…

our civilization. In provoking just such reflection and clarity of definition, the proposal for altered nuclear transfer sets the foundation for a positive future of scientific advance.

Yet, some will say, "How can such a tiny clump of cells hold such significance?"

Three hundred years ago French philosopher-mathematician Blaise Pascal noted that human existence is located between infinities—between the infinitely large and the infinitely small. He went on to say, "By size, the universe surrounds and swallows me up like a dot: by thought I encompass the universe."

But what kind of thought could encompass the universe? That thought must be a moral thought—that thought must be love.

C.S. Lewis once said that we should answer all of our problems with more love, not less love—that precious love that nourished and sustained each one of us in the early dawn of our unfolding form.

Now, as we prepare to enter the future with the new powers of our scientific understanding, we should remember the words of St. John of the Cross: "In the evening of life, we will be judged by love."

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[5]Jaenisch, Rudolf. "Testimony of Rudolf Jaenisch, MD, Hearing on 'An Alternative Method for Obtaining Embryonic Stem Cells," Committee on Appropriations, Subcommittee of Labor, Health, and Human Services, Education. United States Senate Oct. 19, 2005.

***William B. Hurlbut, MD,** is a physician and consulting professor at the Stanford University Medical Center Neuroscience Institute. Dr. Hurlbut has served on the President's Council on Bioethics since 2002. He is a member of the chemical and biological warfare working group at the Center for International Security and Cooperation.*

Editorial

I am so excited to be able to offer our readers the article here from William Hurlbut, MD. As a researcher, a member of the President's Council on Bioethics, and a well-informed theologian, he offers here an eloquent position on the moral status of the human embryo. In addition, he offers a vision for a way forward with research that would be morally acceptable to all parties in our national debate over stem-cell research. He advocates for a particular method of generating stem cells he calls altered nuclear transfer over against somatic cell nuclear transfer, commonly called cloning. To be clear, Dr. Hurlbut is in favor of stem-cell research, but in the effort to protect human life, he wants to use cells generated from the altered nuclear transfer method he describes here. I very much enjoyed his visit to our campus and applaud him in his efforts to find consensus in the national context.

His position on the moral status of the human embryo is clear. After conception, the resultant human life is inviolable. As you know, our Center for Christian Bioethics routinely publishes articles with which we agree and disagree. In fact, among our Seventh-day Adventist readers, many will agree with Dr. Hurlbut and many will disagree. Implicit in the Seventh-day Adventist statement, "Guidelines on Abortion," is a more developmental view of the embryo. Attached to this document is a 12 point statement titled "Principles for a Christian View of Life" (available at <www.adventist.org/beliefs/guidelines/main_guide1.html>). This more developmental view, as some call it, does not seek to denigrate the moral status of the embryo in any way, shape, or form. It does, however, seek to recognize that, in exceptional and tragic circumstances, there may be justifiable reasons to override the moral status of the embryo. What would those circumstances be? In the statement, rape and incest are mentioned as justifiable reasons.

The Seventh-day Adventist Church does not yet have a formal statement on stem-cell research; it is currently working on this issue. A few indicators point in the direction of a position in favor of support for some types of stem-cell research. First, the implicit developmental view thus far taken by the Church leans away from the view of the embryo as inviolable. Second, the direction our healing ministries have taken in the past has blended cutting-edge medical science and technology with our spiritual concern for persons. Third, coupled with our tendency to be on the cutting edge, our intense desire to extend the healing ministry of Jesus inclines us toward the very promising therapies that most believe will come from stem-cell research.

Ours is not a boring time, and those of us here at Loma Linda University and the Center for Christian Bioethics feel privileged to be involved.

Director, Center for Christian Bioethics
Loma Linda University

2006 Contributor's Convocation

"Present Day Health Care: Collaborate or Close the Door"

November 4, 2006
The Mission Inn, Riverside, California

The Riverside location drew a large crowd to the 15th annual Contributor's Convocation. It was a wonderful Sabbath day filled with moments of transformation and enlightenment. Stephen King, senior vice president of mission and ministry, Centura Health; and Ruthita Fike, executive vice president for hospital affairs, Loma Linda University Adventist Health Sciences Center, shared some of the challenges of offering health care as a ministry in a world that is entirely business-oriented.

Two of our students in the master of arts program in biomedical and clinical ethics—George Dzimiri and Whitny Braun—shared a bit of their research, as did the newest members of the School of Religion: Carla Gober, returning to Loma Linda University from Emory University, where she is finishing up her PhD; Andy Lampkin, who comes to us from Oakwood College; and Julius Nam, from Pacific Union College.

Thank you to our 2005–2006 contributors

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"2006 Contributor's Convocation" continued…

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Update
Volume 21, Number 3 (January 2007)

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